Quadrivalent Human Papillomavirus
AGAINST THE MOST COMMON SEXUALLY TRANSMITTED

By Christine A. Garcia, MPH, and Kathe Gustafson, MPH

Human papillomavirus (HPV) is the most common sexually transmitted infection (STI) worldwide, causing genital warts and nearly all cases of cervical cancer. In the United States, it is estimated that 20 million people are currently infected with HPV and that approximately 6.2 million new people will become infected this year (1). Approximately 70 percent of cervical cancers result from infection with HPV genotypes 16 and 18 (2). The American Cancer Society estimates that there will be 9,710 new cases of cervical cancer and 3,700 deaths from cervical cancer in the United States in 2006 (3).

On June 8, 2006, the U.S. Food and Drug Administration (FDA) licensed a live, quadrivalent human papillomavirus vaccine (trade name Gardasil, Merck & Co., Inc.) for use in females age 9–26 years. The Advisory Committee on Immunization Practices (ACIP) voted at their June 2006 meeting to recommend the routine use of quadrivalent HPV vaccine as a three-dose series for females ages 11–12 years. Quadrivalent HPV is also recommended for females ages 13–26 years who did not complete or receive the vaccine when they were younger. The series can be started in females as young as nine years. This article summarizes information about the use of this new vaccine (www.cdc.gov/nip/vfc/acip_vfc_resolutions.htm). When available, ACIP's final recommendations as well as any updated vaccine information will be posted on the CDC website (www.cdc.gov/nip).

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Disease Epidemiology and Vaccine Information

Human papillomavirus types 16 and 18 cause approximately 70 percent of cervical cancer cases along with some cases of the other, less common anogenital cancers and chronic infections of the head and neck. Most HPV infections of the head and neck are not malignant cancers but result in recurrent benign conditions such as warts. HPV types 6 and 11 cause approximately 90 percent of genital warts. Quadrivalent HPV vaccine is a prophylactic vaccine against human papillomavirus type 6, 11, 16, and 18, and is not intended as a treatment for active disease or current infection. The vaccine has not been shown to protect against disease caused by non-vaccine HPV types.

Gardasil is a non-infectious recombinant, quadrivalent vaccine prepared from highly purified virus-like particles (VLPs) of the major capsid (L1) protein of HPV types 6, 11, 16, and 18. The L1 proteins are produced by fermentation in recombinant yeast cells. Quadrivalent HPV vaccine is a sterile liquid suspension that contains the adsorbed VLPs of each HPV type, aluminum-containing adjuvant, and purification buffer, and does not contain any preservative or antibiotics.

In clinical trials, women who were not infected with the HPV types 16 and 18 prior to dose one and through one month post-dose quadrivalent HPV vaccine had an efficacy of 100 percent against high-grade cervical, vulvar, or vaginal precursors [CIN2/3, AIS, VIN2/3, ValN2/3] associated with HPV types 16 and 18. Quadrivalent HPV vaccine had an efficacy of 96 percent against any grade of cervical intraepithelial neoplasia (CIN) [CIN1, CIN2/3] or adenocarcinoma in situ (AIS) related to HPV types 6, 11, 16, and 18. The vaccine had an efficacy of 99 percent against genital warts associated with HPV types 6, 11, 16, and 18. The vaccine does not protect against HPV types acquired prior to vaccination.

Recommendations for Vaccine Use

Routine immunization with three doses of quadrivalent HPV vaccine is recommended for females 11–12 years of age. The series can be started in females as young as nine years of age. Catch-up vaccination is recommended for females 13–26 years of age who have not been vaccinated previously or who have not completed the full vaccine series. Ideally, the vaccine should be administered

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Recombinant Vaccine:
INFECTION WORLDWIDE

before potential exposure to HPV through sexual contact; however, females who are already sexually active should still be vaccinated.

At present, cervical cancer screening recommendations have not changed for females who received the HPV vaccine, as 30 percent of cervical cancers are caused by HPV types that are not prevented by the HPV vaccine. Providers should continue to educate women about the importance of cervical cancer screening. Quadrivalent HPV vaccine should be administered intramuscularly as a series of three separate 0.5 mL doses. The second dose should be given two months after the first dose, and the third dose should be given six months after the first dose. The vaccine may be given at the same

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visit when other age-appropriate vaccines are provided, such as Tdap and MCV4.

Potential Vaccine Reactions

Common Side Effects

The most frequently reported serious adverse events in trials were headache (0.03% vs. 0.03% placebo), gastroenteritis (0.03% vs. 0.01%), appendicitis (0.02% vs. 0.01%), and pelvic inflammatory disease (0.02% vs. 0.01%). Other serious adverse events were rare. Post licensure safety studies will be conducted to more closely assess safety of the vaccine. Minor adverse events reported include pain (84%), swelling (25%), redness (25%), and pruritis (3%) at the injection site. Remember to report suspected reactions to the HPV vaccine or other vaccines to the Vaccine Adverse Events Reporting System (VAERS) at (800) 822-7967 or at http://vaers.hhs.gov.

Contraindications

- History of immediate hypersensitivity to yeast or to any vaccine component is a contraindication.

Precautions

- Quadrivalent HPV vaccine can be administered to females with minor acute illnesses (e.g., diarrhea or mild upper respiratory tract infections, with or without fever).
- Vaccination of people with moderate or severe acute illnesses should be deferred until after the illness improves.

Pregnancy

- Quadrivalent HPV vaccine is not recommended for use in pregnancy. The vaccine has not been associated with adverse outcomes of pregnancy or adverse events to the developing fetus. However, data on vaccination during pregnancy are limited.
- Any exposure to vaccine during pregnancy should be reported to the vaccine pregnancy registry at (800) 986-8999.

Quadrivalent HPV vaccine can be given to females who have an equivocal or abnormal Pap test, a positive Hybrid Capture II(c) high risk test, or genital warts. Vaccine recipients should be advised that data from clinical trials do not indicate the vaccine will have any therapeutic effect on existing Pap test abnormalities, HPV infection, or genital warts. Vaccination of these females would provide protection against infection with vaccine HPV types not already acquired. Females who are immunocompromised either from disease or medication can receive the vaccine; however, the immune response to vaccination and vaccine effectiveness might be less than in females who are immunocompetent. Lactating women can receive quadrivalent HPV vaccine.

Conclusion

For more information, a question and answer sheet on HPV disease, and the HPV vaccine can be found at www.cdc.gov/nip/vaccine/hpv/hpv-faqs.htm. The County of San Diego Health and Human Services Agency Immunization Branch has developed "HPV Vaccine: A Fact Sheet for Providers," which summarizes these recommendations and provides talking points in response to frequently asked parent questions. This document can be accessed at www.sdiz.org in the healthcare provider section or from your immunization management consultant. **SDP**

References

1) Cates W, Jr. Estimates of the incidence and prevalence of sexually transmitted diseases in the United States. American Social Health Association Panel. Sex Transm Dis. 1999; 26(4):Suppl):S2-7.
2) Bosch FX, Manos MM, Munoz N, Sherman M, Jansen AM, Peto J, et al. Prevalence of human papillomavirus in cervical cancer: a worldwide perspective. International biological study on cervical cancer (IBSCC) Study Group. J Natl Inst 1995; 87: 796-802.
3) American Cancer Society. Cancer facts and figures 2006. Atlanta (GA): ACS; 2006. Available at www.cancer.org/downloads/STT/CAFF2006PWSecured.pdf. Retrieved December 12, 2006.

San Diego County Healthcare Stats

San Diego County Immunization Branch conducts an annual random digit dialing (RDD) telephone survey of the residents of San Diego County. One of the surveys conducted this year is that of 582 parents/legal guardians of San Diego County adolescents. The adolescent survey focuses on the immunization status among adolescents age 11–15 years in order to determine vaccination coverage levels for adolescents residing in San Diego County, identify trends between 2003 and 2006, and identify opportunities for new vaccine education (1). Results from the above survey included the following:

- 36.9% of respondents have heard of the new HPV vaccine.
- 59.8% of respondents have never heard of the new HPV vaccine.
- 53% of all respondents would want their child to receive the new HPV vaccine*.
- 36.6% of respondents did not know whether they would want their adolescent to receive the new HPV vaccine*.
- 51.9% of parents/legal guardians would want their daughters to receive the HPV vaccine compared to 39.3% of parents/legal guardians with sons. Parents of adolescent girls were significantly more likely (p-value .010) to want the HPV vaccine for their child (2).

To request additional health statistics describing health behaviors, diseases, and injuries for specific populations, health trends and comparisons to national targets, please call the County's Community Health Statistics Unit at (619) 285-6479. To access the latest data and data links, including the community profiles and the 2004 core public health indicator document, go to www.sdhealthstatistics.com.

* Before responding, those who have never heard of the new vaccine were told the vaccine is used to prevent cervical cancer.

1) RDD Telephone Survey, County of San Diego HHSA Immunization Branch, 2006.
2) Ibid.